

Serial No. 09/074,472



BMID 9619 US

30/F

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: RICHTER, Mark M. *et al.*

Serial No: 09/074,472

Filed: May 7, 1998

For: ASSAYS EMPLOYING
ELECTROCHEMILUMINESCENT LABELS
AND ELECTROCHEMILUMINESCENCE
QUENCHERS

Art Unit: 1655

Examiner: Arun K. Chakrabarti

RECEIVED
MAR 28 2002
TECH CENTER 1600/2900

RESPONSE UNDER 37 CFR §1.116

Assistant Commissioner for Patents
Box AF
Washington, DC 20231

March 22, 2002

Dear Sir:

This reply is in response to the Final Rejection dated November 29, 2001 which has a shortened statutory period for response of three months that expired on February 28, 2002. A Request for Continued Examination and Petition for Extension of Time are enclosed herewith.

AMENDMENT

Please amend the above-identified patent application as shown below.

In the Claims:

In claim 30, paragraph (a), ~~delete~~ “capable of” (2 occurrences).

In claim 30, paragraph (a), ~~change~~ --complimentary-- to “complementary”.

In claim 31, paragraph (a), ~~delete~~ “capable of” (2 occurrences).

In claim 31, paragraph (a), ~~change~~ --complimentary-- to “complementary”.

In claim 32, ~~delete~~ “capable of” (2 occurrences).

In claim 33, ~~delete~~ “capable of” (2 occurrences).

In claim 30, ~~change~~ --complimentary-- to “complementary”.

REMARKS

In view of the comments which follow, and pursuant to 37 CFR §1.116, entry of the above amendment and reconsideration of the Final Rejection of November 29, 2001 is respectfully requested by Applicants.

The claims have been amended by correcting the spelling of “complementary” and by removing the phrase “capable of.” Claims 30-33 remain pending for consideration by the Examiner.

A clean version of the claims and a version with markings to show changes made have been appended hereto.

Objection to claims

Claims 30-33 have been objected to for the use of the term “complimentary”.

Correction of the spelling of “complimentary” to “complementary” has now been made by Applicants, thereby overcoming the Examiner’s objection. Reconsideration of the objection is requested by Applicants.

Rejection under 35 USC §112, second paragraph

Claims 30-33 have been rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner argues that the phrase “capable of” renders the claims indefinite.

Applicants have now deleted all occurrences of the phrase “capable of” to overcome the rejection. The Examiner’s reconsideration of his rejection is respectfully requested.

Rejection 1 under 35 USC §103 (a)

Claims 30-33 have been rejected under 35 USC §103 (a) as being unpatentable over U.S. Patent 6,132,955 issued October 17, 2000 to Talley *et al.* (hereinafter “Talley”) in view of U.S. Patent 5,798,276 issued August 25, 1998 to Haugland *et al.* (hereinafter “Haugland”).

The Examiner argues that Talley teaches a method for quantitative electrochemiluminescence detection of an oligonucleotide target analyte in a sample, the method comprising the steps of:

1. preparing an assay mixture comprising the sample, one or more assay reagents comprising a labeled complex comprising an ECL label selected from ruthenium bipyridine complexes and osmium bipyridine complexes attached

to an oligonucleotide probe complementary to the analyte and capable of hybridizing therewith, the label capable of generating a detectable ECL emission, wherein the labeled complex is immobilized on a magnetic particle, and a coreactant,

2. bringing the assay mixture into contact with a working electrode,
3. applying a potential to the electrode, thereby enabling an ECL reaction to proceed,
4. separating unhybridized labeled complex from hybridized complex,
5. measuring the ECL emission produced by the label hybridized to the analyte via the oligonucleotide probe, and
6. correlating the measured ECL emission with the amount of the analyte in the sample.

The Examiner admits that Talley does not teach a method utilizing a reagent having an ECL quenching moiety, the ECL quenching moiety comprising at least one moiety selected from the group consisting of phenol and benzoquinone.

Haugland, the Examiner argues, teaches a method utilizing a reagent having an ECL quenching moiety (emphasis added by Applicants), the ECL quenching moiety comprising at least one moiety selected from the group consisting of phenol and benzoquinone.

It is the Examiner's position that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to include the group of chemicals containing phenol of Haugland in the method of Talley, since Haugland states "Dyes that are able to preferentially bind to a specific biological ingredient in a sample enable the researcher to determine the presence or quantity of that specific ingredient. In

addition, specific cellular structures can be monitored with respect to their spatial and temporal distribution in diverse environments. Many applications utilize chemically reactive fluorescent dyes by chemically attaching the dye to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or synthetic polymers to make fluorescent conjugates.” The Examiner argues that an ordinary practitioner would have been motivated to combine and compare “the electrochemiluminescence quenching chemicals containing differentially substituted phenol ring of Haugland” (emphasis added by Applicants) into the method of Talley in order to achieve the express advantages, as noted by Haugland, of dyes that are able to preferentially bind to a specific biological ingredient in a sample, which enables the researcher to determine the presence or quantity of that specific ingredient and in addition, to monitor specific cellular structures with respect to their spatial and temporal distribution in diverse environments and in addition has many applications that utilize chemically reactive fluorescent dyes by chemically attaching the dye to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or synthetic polymers to make fluorescent conjugates.

Applicants argue that the Examiner’s case for *prima facie* obviousness has not been made. In making his argument, the Examiner has mischaracterized the dye compounds of Haugland as an “ECL quenching moiety” or “electrochemiluminescence quenching chemicals”, when in fact, Haugland actually teaches fluorescent dyes. Haugland teaches reactive dyes attached to a sulforhodamine 101 fluorophore and conjugates prepared therefrom. Among the advantages of Hauglands derivatives are enhanced solubility and increased fluorescence. (See Abstract.) Thus, the person skilled in the art would have no reason to try to combine a fluorescent dye of Haugland with the electrochemiluminescent method of Talley. Further leading away from such a combination is Haugland’s teaching at column 3, lines 4-9, that there is an unexpected reduction of quenching of the dyes by their conjugates. Finally, Applicants argue that it is

reasonable to expect that the combination of Talley and Haugland would either be inoperable or lack utility as an electrochemiluminescent assay, with which Talley (and the present invention) are concerned.

Applicants argue that the combination of the Talley and Haugland references do not make the claimed invention and that the Examiner's case of *prima facie* obviousness has not been made. Neither of the references teaches or suggests the use of an electrochemiluminescent quencher in an electrochemiluminescence assay for an analyte. The examiner's reconsideration of the rejection of claims 30-33 under 35 USC §103 (a) in light of the above remarks is respectfully requested by Applicants.

Rejection 2 under 35 USC §103 (a)

Claims 30-33 have been rejected under 35 USC §103 (a) as being unpatentable over Talley in view of Haugland and further in view of Stratagene Catalog (1988, page 39, hereinafter "Stratagene").

The Examiner argues that Talley in view of Haugland expressly teaches the method claims and assay reagents of claims 30-31, as described in Examiner's argument above. Talley in view of Haugland do not teach the motivation to combine all the reagents for detecting an analyte in a sample in the form of a kit. Stratagene teaches a motivation to combine reagents into kit format.

It is the Examiner's position that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container, ECL label and ECL quenching moiety of Talley in view of Haugland into a kit format as discussed by Stratagene since Stratagene teaches a motivation for combining reagents for use in an assay into a kit.

Applicants argue that even the combination of all three references still do not make the claimed invention and that the Examiner's case of *prima facie* obviousness has

not been made. None of the references teaches the use of an ECL quencher in an electrochemiluminescence assay for an analyte. The examiner's reconsideration of the rejection of claims 30-33 under 35 USC §103 (a) in light of the above remarks is respectfully requested by Applicants.

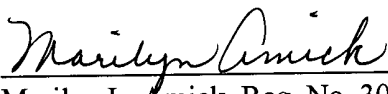
* * * * *

Applicants submit that their application is now in condition for allowance, and entry of the present amendment and favorable reconsideration of their application in light of the above remarks is respectfully requested. Allowance of claims 30-33 at an early date is earnestly solicited.

The Examiner is hereby authorized to charge any fees associated with this amendment to Deposit Account No. 02-2958. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

March 22, 2002


Marilyn L. Amick, Reg. No. 30,444
Roche Diagnostics Corporation
9115 Hague Road
Indianapolis, IN 46250-0457
Phone: 317-521-7561
Fax: 317-521-2883